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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/594,944 | 10/08/2008 | Christopher G.A. McGregor | 630666.00077 | 5774 |

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| EXAMINER | |
|---|---|
| LI, QIAN JANICE | |
| ART UNIT | PAPER NUMBER |
| 1633 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 09/27/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/594,944 | MCGREGOR ET AL. | |
| | Examiner | Art Unit | |
| | Q. JANICE LI | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-17 are pending in the application and under current examination.

### *Specification*

The abstract of the disclosure is objected to because it does not commence on a sheet separate from other materials of the disclosure. Correction is required. See MPEP § 608.01(b). The cover page of a PCT publication is no longer acceptable by the Patent publication branch at the USPTO.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Stone et al.* (USP 6,383,732) view of *Phelps et al.* (Science 2003;299:411-4, IDS).

*Stone* teaches a method of preparing non-immunogenic heart valves from a non-human animal for implanting into a human patient for xenogenic heart valve replacement, and an article of manufacture generated from the process, wherein the non-human animal may be genetically altered animals such as porcine (e.g. column 4, lines 60-67). *Stone* teaches, the invention provides an article of manufacture comprising

a substantially non-immunogenic heart valve xenograft for implantation into humans, wherein the non-immunogenic state was achieved via multiple chemical, enzymatic, and physical approaches (see e.g. the abstract). For example, removing at least a portion of soft tissue from a non-human animal to provide a xenograft; washing the xenograft in saline and alcohol; subjecting the xenograft to cellular disruption treatment (exposure to ultraviolet radiation, immersion in alcohol, ozonation, freeze/thaw cycling and sterilization); treating the xenograft with crosslinking agents such as glutaraldehyde, formaldehyde, adipic dialdehyde, and the like, may be used to crosslink the extracellular collagen of the xenograft (e.g. column 6, lines 9-23), and digesting the xenograft with a proteoglycan-depleting factor and/or glycosidase and various means for deleting $\alpha$1,3-Gal epitope (e.g. columns 7-8). *Stone* also teaches tissue for transplantation is commonly cryopreserved to optimize cell viability during storage, pointing to U.S. Pat. No. 5,071,741; U.S. Pat. No. 5,131,850; U.S. Pat. No. 5,160,313; and U.S. Pat. No. 5,171,660, which disclose art-known cryoprotectants. *Stone* goes on to teach once tissue was removed from the non-human animal, optionally, the valve or valve portions are supported with stents, rings and the like (e.g. column 5, lines 22-30). *Stone* also teaches prior to implantation, the heart valve xenograft may be treated with limited digestion by proteolytic enzymes such as ficin or trypsin to increase tissue flexibility, or coated with anticalcification agents, antithrombotic coatings, antibiotics, growth factors, or other drugs which may enhance the incorporation of the xenograft into the recipient (column 9, lines 33-40). As to various types of heart valves as recited in claims 2-6, they were well known in the art and most mentioned by *Stone* (e.g. column 5, lines 6, 9-11

and 26). Stone did not particularly mention the genetically altered non-human donor may be a pig whose α1,3-Galactosyl-transferase (α1,3-GT) gene has been knocked out.

*Phelps* supplemented *Stone* by establishing a pig deficient in α1,3-Galactosyl-transferase (α1,3-GT) gene had become available before instant priority date. *Phelps* teaches a method of preparing a homozygous knockout pig deficient in α1,3-Galactosyl-transferase (*α1,3-GT-/-*) gene and pigs produced, which lacks α1,3-Gal epitope Galα1,3Galb1,4GlcNac on the surface of endothelial cells (see e.g. the abstract). *Phelps* teaches α1,3-Gal epitope is a major xenoantigen causing hyperacute rejection in pig-to-human xenotransplantation procedures and the availability of the *α1,3-GT-/-* pig provides means to make a safer xenograft product for human use (e.g. the introduction, page 411).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the pig disclosed by *Phelps* in the method taught by *Stone* for preparing a porcine heart valve and using such for xenotransplantation with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to do so because the tissue obtained from the pigs taught by *Phelps* would have depleted a major xenogenic immunogen α1,3-Gal epitope, hence safer for xenotransplantation in humans. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7:30 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

*/Q. JANICE LI/*
*Primary Examiner, Art Unit 1633*

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QL
September 22, 2010